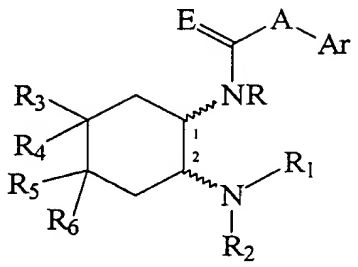
#6/B
6-29-00

WHAT IS CLAIMED IS:

1. An anti-pruritic composition comprising a compound of formula I or a pharmaceutically acceptable salt thereof



I

wherein

the wavy line bond (~) between the nitrogen in the 2-position and the cyclohexyl ring carbon indicates the bond can be either cis- or trans with respect to each substituent on the cyclohexyl ring;

A is a single chemical bond (-), $-(CH_2)_q$, $CH(CH_3)$- or $-X(CH_2)_n$
where q is 1 to 4,
n is 1-4 and
x is O or S;

Ar is an aromatic, hetero-aromatic, bicyclic-aromatic, tricyclic-aromatic group or diphenyl methyl each of which may be unsubstituted or substituted with a member selected from the group consisting of H, halo, trifluoromethyl, nitro, C_1-C_3-alkoxy, hydroxy, azido, C_1-C_3-alkyl, methanesulfonyl, cyano, amino, C_1-C_3-alkoxycarbonyl, C_1-C_3-alkanoyloxy, and C_1-C_3-carboxacylamino of the formula $-NHC(O)R_7$
where R_7 is H, C_1-C_2-alkyl, and aromatic or hetero-aromatic group;

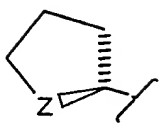
R_1 and R_2 are independently H, C_1-C_3-alkyl or allyl;

R_1 and R_2, taken together with the nitrogen to which they are bonded, complete a ring selected from the group consisting of azetidinyl, pyrrolidinyl, 3-hydroxypyrrolidinyl, 3-fluoropyrrolidinyl, morpholinyl, piperidinyl, and 3,4-dehydropiperidinyl;

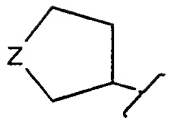
R_3, R_4, R_5, R_6 are independently H, hydroxy, OR_8 or $OC(=O)R_9$;

R_5 and R_6 taken together may form the group $-E-CH_2-CH_2-E-$;

R_5 and R_6 taken together may form a ring



or



where

Z is selected from the group consisting of oxygen (-O-), NR_{10}, sulfur (-S-), sulfinyl (-S(O)-), and sulfonyl ($-S(O)_2-$);

E is N~OH, N~OC(O)CH_3, O, S, with the proviso that when E is bivalent sulfur or oxygen, R_5 and R_6 cannot both be hydrogen;

R_8 is C_1-C_3-alkyl;

R_9 is H or C_1-C_3-alkyl;

R_{10} is H, or C_1-C_3-alkyl,

in a pharmaceutically acceptable carrier.

2. The anti-pruritic pharmaceutical composition of claim 1 wherein Ar is pyridine, thiophene, naphthalene, benzofuran, benzothiophine anthracene or fluorene; and halo is F, Cl, Br or I.

3. The anti-pruritic pharmaceutical composition of claim 1 wherein said compound is selected from the group consisting of:

(±)-N-[2-(N,N'-dimethylamino)cyclohexyl]-N-methyl-2-(4-trifluoromethylphenyl)acetamide;
(±)-N-[2-(N',N'-dimethylamino)cyclohexyl]-N-propyl-2-(3-methoxyphenyl)acetamide;
(±)-N-[2-(N',N'-dimethylamino)cyclohexyl]-N-methyl-2-(4-azidopbenyl)acetamide;
(±)-N-[2-(N',N'-dimethylamino)cyclohexyl]-N-methyl-2-(3,4-dichlorophenyl)acetamide;
(±)-N-[2-(N',N'-dimethylamino)cyclohexyl]-N-methyl-2-(4-methoxyphenyl)acetamide;
(±)-N-[2-(N',N'dimethylamino)cyclohexyl]-N-methyl-2-(2-naphthyl)acetamide;
(±)-N-[2-(N-cyclopropyl-N-methylamino)cyclohexyl]-2-(4-azidophenyl)acetamide;
(±)-N-(2-(3-acetoxy-1-pyrrolidinyl)cyclohexyl]-N-methyl-2-(3,4-dichlorophenyl)acetamide;
(±)-N-[2-(N-pyrrolidinyl)cyclohexyl]-N-methyl-2-(3,4-dichlorophenyl)acetamide;
(±)-N-[2-(3-hydroxypyrrolidinyl)cyclohexyl]-N-methyl-2-(3,4-dichlorophenyl)acetamide;
(±)-N-[2-[N'-(3-hydroxy-1-azetidinyl]cyclohexyl]methyl-2-(3,4-dichlorophenyl)acetamide;

(±)-N-[2-(N',N'-diethylamino)cyclohexyl]-N-methyl-2-(3,4-dichlorophenyl)acetamide;
(±)-N-[2-(N'-pyrrolidinyl)cyclohexyl]-N-methyl-2-(3,4-dichlorophenyl)propionamide;
(±)-N-[2-(4-methyl-1-piperazinyl)cyclopentyl]-2-(3,4-dichlorophenyl)acetamide;
(±)-N-[2-(N,N-dimethylamino)cyclohexyl]-2-(3,4-dichlorophenyl)acetamide;
(±)-3,4-dichloro-N-methyl-N-[8-(1-pyrrolidinyl)-1,4-dioxaspiro[4.5]dec-7-yl]-benzeneacetamide;
(±)-3,4-dichloro-N-methyl-N-[7-(1-pyrrolidinyl)-1,4-dioxaspiro[4.5]dec-8-yl]-benzeneacetamide;
(±)-3,4-dichloro-N-methyl-N-[7-(1-pyrrolidinyl)-1,4-dioxaspiro[4.5]dec-6-yl]-benzeneacetamide;
(±)-4-bromo-N-methyl-N-[7-(1-pyrrolidinyl)-l,4-dioxaspiro[4.5]dec.8.yl]-benzeneacetamide;
(±)-3.fluoro-Nethyl-N-[7-(l-azetidinyl)-1,4-dioxaspiro[4.5]dec-8-yl]benzeneacetamide;
(±)-3,4-dichloro-N-methyl-N-[7-(1-pyrrolidinyl)-1,4-dioxaspiro[4.4]-non-8-yl)-benzeneacetamide;
(±)-3,4-dichloro-N-methyl-N-[7-(l-pyrrolidinyl)-1,4-dioxaspiro[4.6]-undec-8-yl]-benzeneacetamide;
(±)-3,4-dichlor-N-methyl-N-[8-(1-pyrrolidinyl)-1,4-dioxaspiro[4.6]-undec-7-yl]-benzeneacetamide;
(±)-3,4-dichloro-N-methyl-N-[9-(1-pyrrolidinyl)- 1,4-dioxaspiro[4.6]-undec-8-yl]-benzeneacetamide;
(±)-3,4-dichloro-N-[4-methoxy-2-(1-pyrrolidinyl)cyclohexyl]-N-methylbenzeacetamide;
(±)-3,4-dichloro-N-[5-methoxy-2-(1-pyrrolidinyilcyclohexyll-N-methylbenzeneacetamide;
(±)-3,4-dichloro-N-methyl-N-[4-oxo-2-(1-pyrrolidinyl)cyclohexyl]-benzeneacetamide;
(±)-4-bromo-N-methyl-N-[2-(N',N'-dimethylamino)-4-oxo-cyclohexyl]benzeneacetamide;
(±)-N-[4-acetyloxy-2-(1-pyrrolidiny])cyclohexyl]-3,4-dichloro-N-methylbenzeneacetamide;
(±)-N-[4-acetyloxy-2-aminocyclohexy1]-3,4-difluoro-N-methylbenzeneacetarnide;
(±)-3,4-dichloro-N-[5-(hydroxyimino)-2-(1-pyrrolidinyl)cyclohexyl]-N-methylbenzeneacetamide;
(±)-3,4-dichloro-N-[4,4-dimethoxy-2-(1-pyrrolidinyl)cyclohexyl]-N-methylbenzeneacetamide which can also be named:
(±)-3,4-dichloro-N-methyl-N-[4-oxo-2-(1-pyrrolidinyl)cyclohexyllbenzeneacetamide, dimethyl ketal;
(±)-3,4-dichloro-N-[5,5-diethoxy-2-(1-pyrrolidinyl)cyclohexyl]-N-methylbenzeneacetamide;
(±)-(1α, 2β)-3,4-dichloro-N-[4,4-dimethoxy-2-(1-pyrrolidinyl)cyclohexyl]-N-methyl benzeneacetamide;
(±)-4-trifluoromethyl-N-[4,4-dimethoxy-2-(1-pyrrolidinyl)cyclohexyl]-N-methylbenzeneacetamides ;
(±)-3-trifluoromethyl -N-[4,4-diethoxy-2- (1-pyrrolidinyl)-cyclohexyl]-N-methylbenzeneacetamide;
(±)-3-hydroxy-4-methyl-N-[4,4-dimethoxy-2-(1-pyrrolidinyl)cyclohexyl]-N-methylbenzeneacetamide;

(±)-4-methanesulfonyl-N-[4,4-dimethoxy-2-(l-piperidinyl)-cyclohexyl]-N-methylbenzamide;
(±)-4- acetyloxy-N-[4,4-dimethoxy-2- (1-pyrrolidinyl)-cyclohexyl-N-methylbenzeneacetamide;
(±)-N-[4,4-bis(methylthio)-2-(l-pyrrolidinyl)cyclohexyl]-3,4-dichloro-N-methylbenzeneacetamide;
(±)-N-[5,5-bis(ethylthio)-2-(l-pyrrolidinyl)cyclohexyl]-3,4-di-chloro-N-methylbenzeneacetamide;
(±)-3,4-dichloro-N-[4-methylthio-2-(1-pyrrolidinyl)cyclohexyl]-N-methylbenzeneacetamide;
(±)-3,4-dichloro-N-[5-ethylthio-2-(1-pyrrolidinyl)cyclohexyl]-N-methylbenzeneacetamide;
(±)-3,4-dichloro-N-[6-methylthio-2-(l-pyrrolidinyl)cycloheptyl]-N-methylbenzeneacetamide;
(±)-3,4-dichloro-N-[4-mercapto-2-(l-pyrrolidinyl)cyclohexyl]-N-methylbenzeneacetamide;
[1R-(1α,2β,4β,5β)]-N-[4,5-dimethoxy-2-(1-pyrrolidinyl)cyclohexyl]-N-methyl-4-benzofuranacetamide;
[1S-(1α,2β,4β,5β)]-N-[4,5-dimethoxy-2-(1-pyrrolidinyl)cyclohexyl]-N-methyl-4-benzofuranacetamide;
[1R-(1α,2β,4α,5α)]-N-[4,5-dimethoxy-2-(1-pyrrolidinyl)cyclohexyl]-N-methyl-4-benzofuranacetamide;
[1S-(1α,2β,4α,5α)]-N-[4,5-dimethoxy-2-(1-pyrrolidinyl)cyclohexyl]-N-methyl-4-benzofuranacetamide;
[1R-(1α,2β,4β,5β)]-N-[4,5-dimethoxy-2-(1-pyrrolidinyl)cyclohexyl]-N-methyl-benzo[b]thiophene-4-acetamide;
[1S-(1α,2β,4β,5β)]-N-[4,5-dimethoxy-2-(1-pyrrolidinyl)cyclohexyl]-N-methyl-benzo[b]thiophene-4-acetamide;
[1R-(1α,2β,4α,5α)]-N-[4,5-dimethoxy-2-(1-pyrrolidinyl)cyclohexyl]-N-methyl-benzo[b]thiophene-4-acetamide;
[1S-(1α,2β,4α,5α)]-N-[4,5-dimethoxy-2-(1-pyrrolidinyl)cyclohexyl]-N-methyl-benzo[b]thiophene-4-acetamide;
[1R-(1α,2β,4β,5β)]-N-[4,5-dimethoxy-2-(1-pyrrolidinyl)cyclohexyl]-N-methyl-1-naphthaleneacetamide;
[1S-(1α,2β,4β,5β)]-N-[4,5-dimethoxy-2-(1-pyrrolidinyl)cyclohexyl]-N-methyl-1-naphthaleneacetamide;
[1R-(1α,2β,4α,5α)]-N-[4,5-dimethoxy-2-(1-pyrrolidinyl)cyclohexyl]-N-methyl-1-naphthaleneacetamide;
[1S-(1α,2β,4α,5α)]-N-[4,5-dimethoxy-2-(1-pyrrolidinyl)cyclohexyl]-N-methyl-1-naphthaleneacetamide;
[1R-(1α,2β,4β,5β)]-3,4-dichloro-N-[4,5-dimethoxy-2-(1-pyrrolidinyl)cyclohexyl]-N-methybenzeneacetamide;
[1S-(1α,2β,4β,5β)]-3,4-dichloro-N-[4,5-dimethoxy-2-(1-pyrrolidinyl)cyclohexyl]-N-methybenzeneacetamide;

[1R-(1α,2β,4α,5α)]-3,4-dichloro-N-[4,5-dimethoxy-2-(1-pyrrolidinyl)cyclohexyl]-N-methybenzeneacetamide;
[1S-(1α,2β,4α,5α)]-3,4-dichloro-N-[4,5-dimethoxy-2-(1-pyrrolidinyl)cyclohexyl]-N-methybenzeneacetamide;
[1R-(1α,2β,4β,5β)]-N-[4,5-dimethoxy-2-(1-pyrrolidinyl)cyclohexyl]-N-methyl-9H-fluorene-9-carboxamide;
[1S-(1α,2β,4β,5β)]-N-[4,5-dimethoxy-2-(1-pyrrolidinyl)cyclohexyl]-N-methyl-9H-fluorene-9-carboxamide;
[1R-(1α,2β,4α,5α)]-N-[4,5-dimethoxy-2-(1-pyrrolidinyl)cyclohexyl]-N-methyl-9H-fluorene-9-carboxamide;
[1S-(1α,2β,4α,5α)]-N-[4,5-dimethoxy-2-(1-pyrrolidinyl)cyclohexyl]-N-methyl-9H-fluorene-9-carboxamide;
(±)-(1α,2β,4β)-N-methyl-N-[4-methoxy-2-(1-pyrrolidinyl)cyclohexyl]-4-benzofuranacetamide;
(±)-(1α,2β,4α)-N-methyl- N-[4-methoxy-2-(1-pyrrolidinyl)cyclohexyl]-4-benzofuranacetamide;
(±)-(1α,2β,5β)-N-methyl-N-[5-methoxy-2-(1-pyrrolidinyl)cyclohexyl]-4-benzofuranacetamide;
(±)-(1α,2β,5α)-N-methyl- N-[5-methoxy-2-(1-pyrrolidinyl)cyclohexyl]-4-benzofuranacetamide;
(±)-(1α,2β,4α)-N-[4-methoxy-2-(1-pyrrolidinyl)cyclohexyl]-N-methyl-9H-fluorene-9-carboxamide;
(±)-(1α,2β,5β)-N-[5-methoxy-2-(1-pyrrolidinyl)cyclohexyl]-N-methyl-9H-fluorene-9-carboxamide;
(±)-N-methyl-2-(1-naphthalenyloxy)-N-[2-(1-pyrrolidinyl)cyclohexyl]acetamide;
(±)-N-methyl-2-(2-naphthalenyoxy)-N-[2-(1-pyrrolidinyl)cyclohexy]jacetamide;
(±)-1,2-dihydro-N-methyl-N-[2-(1-pyrrolidinyl)cylohexyl]-l-acenaphthylencarboxamide, (isomer I, mixture of (1α, 2β) and (1β,2α) forms);
(±)-1,2-dihydro-N-methyl-N-[2-(1-pyrrolidinyl)cyclohexyl]-1-acenaphthylenecarboxamide, (isomer II, mixture of (1α, 2β) and (1β,2α) forms);
(±)-N-[4,5-dimethoxy-2-(1-pyrrolidinyl)cyclohexyl]-1,2-dihydro-N-methyl-1-acenaphthylenecarboxamide (isomer I, mixture of (1α,2β, 4β, 5β) and (1β, 2α, 4α, 5α forms);
(±)-N-[4,5-dimethoxy-2-(1-pyrrolidinyl)cyclohexyl]-1,2-dihydro-N-methyl-l-acenaphthylenecarboxamide (isomer II, mixture of (1α,2β, 4β, 5β) and (1β, 2α, 4α, 5α forms);
(±)-1,2-dihydro-N-[4-methoxy-2-(1-pyrrolidinyl)cyclohexyl]-N-methyl-l-acenaphthylenecarboxamide (isomers I and II, mixtures of (1α,2β, 4β) and (1β, 2α, 4α) forms);
(±)-1,2-dihydro-N-[4-methoxy-2-(1-pyrrolidinyl)cyclohexyl]-N-methyl-l-acenaphthylenecarboxamide (isomers I and 11, mixtures of (1β, 2α, 4α) and (1α,2β, 4β) forms);
(±)-trans-N-methyl-N-[2-(1-pyrrolidinyl)cyclohexyl]-9H-fluorene-9-carboxamide;
(±)-trans-1,3-dihydro-N-methyl-1-oxo-N-[2-(1pyrrolidinyl)cyclohexyl]-4-isobenzofuranacetamide;
(±)-(1α,2β, 4β, 5β)-N-[4,5-dimethoxy-2-(1-pyrrolidinyl)cyclohexyl]-1,3-dihydro-N-methyl-1-oxo-4-isobenzofuranacetamide;
(±)-(5α,7α, 8β)-3,4-dichloro-N-methyl-N-[7-(1-pyrrolidinyl)-1-oxaspiro[4.5]dec-8-yl] benzeneacetamide;

(±)-(5α,7α, 8β)-bromo-N-methyl-N-[7-(1-pyrrolidinyl)-1-oxaspiro[4.5]dec-8-yl] benzeneacetamide;
(±)-(5α,7α, 8β)-4-methoxy-N-methyl-N-[7-(1-pyrrolidinyl)-1-oxaspiro[4.5]dec-8-yl] benzeneacetamide;
(±)-(5α,7α, 8β)-N-methyl-2-nitro-N-[7-(1-pyrrolidinyl)-1-oxaspiro[4.5]dec-8-yl] benzeneacetamide;
(±)-(5α,7α, 8β)-N-methyl-3-nitro-N-[7-(1-pyrrolidinyl)-1-oxaspiro[4.5]dec-8-yl] benzeneacetamide;
(±)-(5α,7α, 8β)-N-methyl-4-nitro-N-[7-(1-pyrrolidinyl)-1-oxaspiro[4.5]dec-8-yl] benzeneacetamide;
(±)-(5α,7α, 8β)-N-methyl-N-[7-(1-pyrrolidinyl)-1-oxaspiro[4.5]dec-8-yl]-3-(trifluoromethyl)benzeneacetamide;
(±)-(5α,6α, 7β)-3,4-dichloro-N-methyl-N-[7-(1-pyrrolidinyl)-1-oxaspiro[4.5]dec-6-yl] benzeneacetamide;
(±)-(5α,7α, 8β)-3,4-dichloro-N-methyl-N-[7-(1-pyrrolidinyl)-1-thiaspiro[4.5]dec-8-yl] benzeneacetamide;
(±)-(5α,7β, 8α)-3,4-dichloro-N-methyl-N-[8-(1-pyrrolidinyl)-1-oxaspiro[4.5]dec-7-yl] benzeneacetamide;
(±)-(5α,7α, 8β)-3,4-dichloro-1,N-dimethyl-[7-(1-pyrrolidinyl)-1-azaspiro[4.5]dec-8-yl] benzeneacetamide;
(±)-(5α,7α, 8β)-4-bromo-N-methyl-N-[7-(1-pyrrolidinyl)-1-azaspiro[4.5]dec-8-yl] benzamide;
(±)-(5α,7α, 8β)-3,4-dichloro-N-methyl-N-[7-(1-pyrrolidinyl)-1-thiaspiro[4.5]dec-8-yl] benzamide;
(±)-(5α,7α, 8β)-3,4-dichloro-N-methyl-N-[7-(1-pyrrolidinyl)-1-thiaspiro[4.5]dec-8-yl] benzeneacetamide;
(±)-(5α,7α, 8β)-3,4-dichloro-N-methyl-N-[7-(1-pyrrolidinyl)-1-thiaspiro[4.5]dec-8-yl] benzeneacetamide, 1-oxide;
(±)-(5α,7α, 8β)-3,4-dichloro-N-methyl-N-[7-(1-pyrrolidinyl)-1-thiaspiro[4.5]dec-8-yl] benzeneacetamide, 1,1-dioxide;
(±)-(5α,7α, 8β)-N-methyl-N-[7-(1-pyrrolidinyl)-1-azaspiro[4.5]dec-8-yl]4-trifluoromethylbenzeneacetamide;
(±)-(5α,7α, 8β)-N-methyl-N-[8-(1-pyrrolidinyl)-1-thiaspiro[4.5]dec-7-yl]-3-trifluoromethylbenzeneacetamide;
[5R-(5α,7α,8β)]-N-Methyl-[7-(1-pyrrolidinyl)-l-oxaspiro[4.5]dec-8-yl]-1H-indene-3-acetamide;
[5S-(5α,7α,8β)]- N-Methyl-[7-(1-pyrrolidinyl)-l-oxaspiro[4.5]dec-8-yl]-lH-indene-3-acetamide;
[5R-(5α,7β,8α)]- N-Methyl-[7-(1-pyrrolidinyl)-l-oxaspiro[4.5]dec-8-yl]-lH-indene-3-acetamide;
[5S-(5α,7β,8α)]- N-Methyl-[7-(1-pyrrolidinyl)-l-oxaspiro[4.5]dec-8-yl]-lH-indene-3-acetamide;
[5R-(5α,7α,8β)]-N-Methyl-N-[7-(1-pyrrolidinyl)-l-oxaspiro[4.5]dec-8-yl]-lH-indole-3-acetamide;
[5S-(5α,7α,8β)]-N-Methyl-N-[7-(1-pyrrolidinyl)-l-oxaspiro[4.5]dec-8-yl]-lH-indole-3-acetamide;
[5R-(5α,7β,8α)]- N-Methyl-N-[7-(l-pyrrolidinyl)-l-oxaspiro[4.5]dec-8-yl]-lH-indole-3-acetamide;
[5S-(5α,7β,8α)]- N-Methyl-N-[7-(l-pyrrolidinyl)-l-oxaspiro[4.5]dec-8-yl]-lH-indole-3-acetamide;
[5R-(5α,7α,8β)]-N-Methyl-N-[7-(l-pyrrolidinyl)-l-oxaspiro[4.5]dec-8-yl]-2-benzofuranacetamide;
[5S-(5α,7α,8β)]-N- Methyl-N-[7-(l-pyrrolidinyl)-l-oxaspiro[4.5]dec-8-yl]-2-benzofuranacetamide;

[5R-(5α,7β,8α)]-N-Methyl-N-[7-(1 -pyrrolidinyl)-1 -oxaspiro[4.5]dec-8-yl]-2-benzo[b]furanacetamide;
[5S-(5α,7β,8α)]-N-Methyl-N-[7-(1 -pyrrolidinyl)-1 -oxaspiro[4.5]dec-8-yl]-2-benzo[b]furanacetamide;
[5R-(5α,7α,8β)]-N-Methyl-N-[7-(1-pyrrolidinyl)-1-oxaspiro[4.5]dec-8-yl]-3-benzo[b]furanacetamide;
[5S-(5α,7α,8β)]-N- Methyl-N-[7-(1-pyrrolidinyl)-1-oxaspiro[4.5]dec-8-yl]-3-benzo[b]furanacetamide;
[5R-(5α,7β,8α)]-N-Methyl-N-[7-(1 -pyrrolidinyl)-1 -oxaspiro[4.5]dec-8-yl]-3-benzo[b]furanacetamide;
[5S-(5α,7β,8α)]-N-Methyl-N-[7-(1 -pyrrolidinyl)-1-oxaspiro[4.5]dec-8-yl]-3-benzo[b]furanacetamide;
[5R-(5α,7α,8β)]-N-Methyl-N-[7-(1-pyrrolidinyl)-1-oxaspiro[4.5]dec-8-yl]-4-benzo[b]furanacetamide;
[5S-(5α,7α,8β)]-N- Methyl-N-[7-(1-pyrrolidinyl)-1-oxaspiro[4.5]dec-8-yl]-4-benzo[b]furanacetamide;
[5R-(5α,7β,8α)]-N-Methyl-N-[7-(1 -pyrrolidinyl)-1-oxaspiro[4.5]dec-8-yl]-4-benzo[b]furanacetamide;
[5S-(5α,7β,8α)]-N-Methyl-N-[7-(1 -pyrrolidinyl)-1-oxaspiro[4.5]dec-8-yl]-4-benzo[b]furanacetamide;
[5R-(5α,7α,8β)]-N-Methyl-N-7-(1-pyrrolidinyl)-1-oxaspiro[4.5]dec-8-yl-4-benzo[b]thiophene-4-acetamide;
[5S-(5α,7α,8β)]- N-Methyl-N-7-(1-pyrrolidinyl)-1-oxaspiro[4.5]dec-8-yl-4-benzo[b]thiophene-4-acetamide;
[5R-(5α,7β,8α)]- N-Methyl-N-7-(1-pyrrolidinyl)-1-oxaspiro[4.5]dec-8-yl-4-benzo[b]thiophene-4-acetamide;
[5S-(5α,7β,8α)]- N-Methyl-N-7-(1-pyrrolidinyl)-1-oxaspiro[4.5]dec-8-yl-4-benzo[b]thiophene-4-acetamide;
(-)-(5α,7α,8β)]-N- Methyl-N-[7-(1-pyrrolidinyl)-1-oxaspiro[4.5]dec-8-yl]-4-benzo[b]furanacetamide;
(-)-(5α,7α,8β)]-N-7-(1-pyrrolidinyl)-1-oxaspiro[4.5]dec-8-yl-4-benzo[b]thiophene-4-acetamide;
(±)-(5α,6α,7β)-3,4-dichloro-N-methyl-N-[7-(1-pyrrolidinyl)-2-oxaspiro[4.5]dec-6-yl] benzeneacetamide;
(±)-(5α,6α,7β)-3,4-dichloro-N-methyl-N-[6-(1-pyrrolidinyl)-2-oxaspiro[4.5]dec-7-yl] benzeneacetamide; and
(±)-(5α,7α,8β)-3,4-dichloro-N-methyl-N-[8-(1-pyrrolidinyl)-2-oxaspiro[4.5]dec-7-yl] benzeneacetamide.

4. A method for the prevention or treatment of pruritus in a mammal in need of such prevention or treatment comprising administering to said mammal an effective anti-pruritic amount of a composition of claim 1.

5. A method for the prevention or treatment of pruritus in a mammal in need of such prevention or treatment comprising administering to said mammal an effective anti-pruritic amount of a composition of claim 2.

6. A method for the prevention or treatment of pruritus in a mammal in need of such prevention or treatment comprising administering to said mammal an effective anti-pruritic amount of a composition of claim 3.

7. The method of claim 4 wherein said administration is topical administration.

8. The method of claim 4 wherein said administration is parenteral administration.

9. The method of claim 4 wherein said administration is oral administration.

10. The method of claim 4 wherein said administration is rectal administration.

11. The method of claim 5 wherein said administration is topical administration.

12. The method of claim 5 wherein said administration is parenteral administration.

13. The method of claim 5 wherein said administration is oral administration.

14. The method of claim 5 wherein said administration is rectal administration.

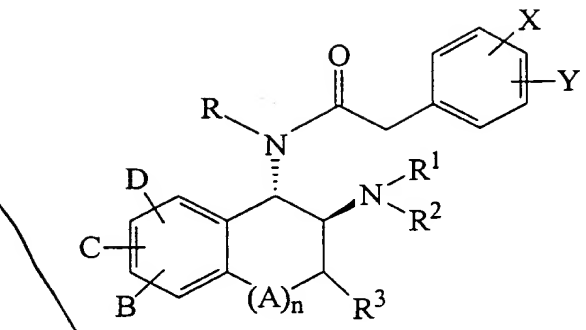
15. The method of claim 6 wherein said administration is topical administration.

16. The method of claim 6 wherein said administration is parenteral administration.

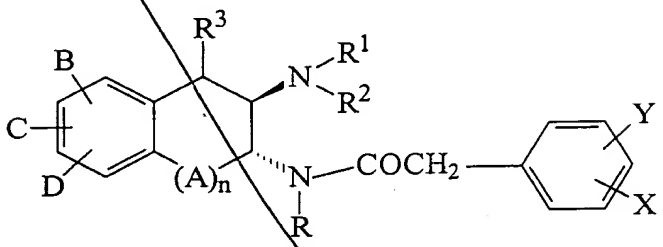
17. The method of claim 6 wherein said administration is oral administration.

18 The method of claim 6 wherein said administration is rectal administration.

19. An anti-pruritic pharmaceutical composition comprising a compound of formulae II or IIa or a stable N-oxide pharmaceutically acceptable salt thereof



II

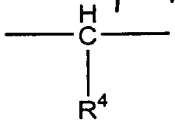


IIa

wherein for the enantiomers and racemic mixtures

n is 0 or 1;

A is



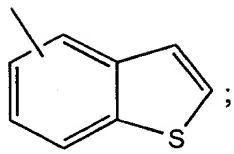
or, $-CH_2CH_2-$ provided that in Formula II, when n is 1, A may also be -O- or -S-;

B, C and D are independently selected from the group consisting of H, OH, $OCOR^5$, $OCH_2CH_2OR^5$, OR^6, R^6, CH_2OR^6, CH_2COR^7, Cl, F, Br, I, NH_2, NHR^8, NR^8R^9, SH, SR^6, CH_2SR^6 and $OC(S)N(CH_3)_2$; or

two of B, C and D when on adjacent carbon atoms taken together form a fused benzo ring;

X and Y are independently selected from the group consisting of H, OCH_3, Cl, F, Br, I, NO_2, CF_3, CN, SO_2R^{10}, and SO_2CF_3; or

X and Y taken together with the benzene ring form



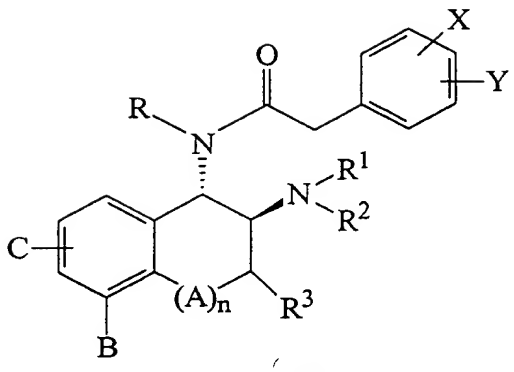
R and R^1 independently are selected from the group consisting of H, and alkyl of 1 to 3 carbon atoms;

R^2 is H; alkyl of 1 to 6 carbon atoms; CH_2CF_3; alkenylmethyl of 3 to 6 carbon atoms; hydroxyalkenylmethyl of 2 to 5 carbon atoms; cycloalkyl of 3 to 6 carbon atoms; cyclopropylmethyl; cyclobutylmethyl, or phenylalkyl of 7 to 9 carbon atoms; or R^2 can be taken together with R^1 and the nitrogen to which they are attached to form 1-azetidinyl, 1-pyrrolidinyl optionally substituted at the 3-position by OH, alkyl of 1 to 3 carbon atoms, alkoxy of 1 to 3 carbon atoms or alkanoyloxy of 1 to 3 carbon atoms; 1-piperazinyl optionally substituted at the 4-position by alkyl of 1 to 3 carbon atoms; 1-morpholino; 2,5-dihydro-1H-pyrrol-1-yl; 3-azabicyclo[3.1.0]hexan-3-yl; or 3-azabicyclo[3.2.0]hoptan-3-yl;

R^3 is H, but if n is 1 and A is CH_2, R^3 may also be CH_3, CH_2OH, CHO, or COR^{11};
R^4 is H, alkyl of 1 to 6 carbon atoms, $-CH_2OH$-, CHO, or COR^{12};
R^5 is alkyl of 1 to 6 carbon atoms, phenyl, or mono-substituted phenyl;
R^6, R^8, R^9, R^{10} and R^{13} are independently an alkyl group of 1 to 3 carbon atoms; and
R^7, R^{11} and R^{12} independently are selected from the group consisting of H, OH, OR^{13}, NHR^{13}, and NR_2^{13};

in a pharmaceutically acceptable vehicle.

20. An anti-pruritic pharmaceutical composition comprising a compound of formulae IIb or a stable N-oxide pharmaceutically acceptable salt thereof



IIb

wherein
n is 1;

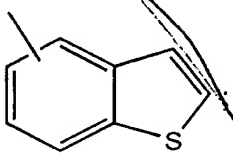
A is $-CH_2-$, -O-, or -S-;

B is OH, $OCOR^5$, $OCH_2CH_2OR^5$, OR^6, CH_2OR^6, or CH_2COR^7;

C is H, OH, or OR^6;

R^1 and R^2 independently are selected from H or alkyl of 1 to 3 carbon atoms or are taken together with the nitrogen to which they are attached to form the group 1-azetidinyl, 1-pyrrolidinyl, 1-(2,5-dihydro-1H-pyrrolyl) or 1-piperidinyl;

X and Y taken together with the benzene ring form



R is H, and C_1-C_3 alkyl;
R^3 is H; and
R^5, R^6 and R^7 are independently C_1-C_3 alkyl,

in a pharmaceutically acceptable carrier.

21. The anti-pruritic pharmaceutical composition of claim 19 wherein said compound is selected from the group consisting of:

(±)trans-3,4-dichloro-N-methyl-N-[2-(pyrrolidin-1-yl)-5-methoxy-1,2,3,4-tetrahydronaphth-1-yl]-benzeneacetamide hydrochloride or the methansulfonic acid salt;

(±)trans-3,4-dichloro-N-methyl-N-[2-(pyrrolidin-1-yl)-1,2,3,4-tetrahydronaphth-1-yl]-benzeneacetamide hydrochloride;

(±)trans-3,4-dichloro-N-methyl-N-[2-(pyrrolidin-1-yl)-6-methoxy-1,2,3,4-tetrahydronaphth-1-yl]-benzeneacetamide hydrochloride;

(±)trans-3,4-dichloro-N-methyl-N-[2-(pyrrolidin-1-yl)-6-hydroxy-1,2,3,4-tetrahydronaphth-1-yl]-benzeneacetamide hydrochloride;

(±)-trans-3,4-dichloro-N-methyl-N-[2-(pyrrolidin-1-yl)-1,2,3,4-tetrahydronaphth-1-yl]-benzeneacetamide hydrochloride;

(±)trans-3,4-dichloro-N-methyl-N-[2,3-dihydro-2-(pyrrolidin-1-yl)-1H-inden-1-yl]-benzeneacetamide hydrochloride;

(±)trans-3,4-dichloro-N-methyl-N-[3,4-dihydro-3-(pyrrolidin-1-yl)-2H-benzopyran-4-yl]-benzeneacetamide hydrochloride;

(±)trans-3,4-dichloro-N-methyl-N-[2-(pyrrolidin-1-yl)-5-hydroxy-1,2,3,4-tetrahydronaphth-1-yl]-benzeneacetamide hydrochloride;

(±)trans-3,4-dichloro-N-methyl-N-[2-(pyrrolidin-1-yl)-5-propionyloxy-1,2,3,4-tetrahydronaphth-1-yl]-benzeneacetamide hydrochloride;

(±)trans-3,4-dichloro-N-methyl-N-[2-(pyrrolidin-1-yl)-5-benzoyloxy-1,2,3,4-tetrahydronaphth-1-yl]-benzeneacetamide hydrochloride;

(±)trans-3,4-dichloro-N-methyl-N-[2-(pyrrolidin-1-yl)-6,7-dihydroxy-1,2,3,4-tetrahydronaphth-1-yl]-benzeneacetamide hydrochloride;

(±)trans-N-methyl-N-[3,4-dihydro-3-(pyrrolidin-1-yl)-2H-benzopyran-4-yl]-benzeneacetamide hydrochloride;

(±)trans-3,4-dichloro-N-methyl-N-[3,4-dihydro-8-methoxy-3-(pyrrolidin-1-yl)-2H-benzopyran-4-yl]-benzeneacetamide hydrochloride;

(±)trans-3,4-dichloro-N-methyl-N-[2-(pyrrolidin-1-yl)-5-(N,N-dimethylthiocarbamoyloxy)-1,2,3,4-tetrahydronaphth-1-yl]-benzeneacetamide hydrochloride;

(±)trans-3,4-dichloro-N-methyl-N-[2-(2,5-dihydro-1H-pyrrol-1-yl)-5-methoxy-1,2,3,4-tetrahydronaphth-1-yl]-benzeneacetamide hydrochloride, and

(±)trans-3-nitro-N-methyl-N-[2,3-dihydro-2-(pyrrolidin-1-yl)-1H-inden-1-yl]-benzeneacetamide hydrochloride.

22. A method for the prevention or treatment of pruritus in a mammal in need of such prevention or treatment comprising administering an effective anti-pruritic amount of the composition of claims 19.

23. A method for the prevention or treatment of pruritus in a mammal in need of such prevention or treatment comprising administering an effective anti-pruritic amount of the composition of claims 20.

24. A method for the prevention or treatment of pruritus in a mammal in need of such prevention or treatment comprising administering an effective anti-pruritic amount of the composition of claims 21.

25. The method of claim 22 wherein said administration is topical administration.

26. The method of claim 22 wherein said administration is parenteral administration.

27. The method of claim 22 wherein said administration is oral administration.

28. The method of claim 22 wherein said administration is rectal administration.

29. A method for the prevention and treatment of pruritus in a mammal in need of such prevention or treatment comprising administering to said mammal an effective anti-pruritic amount of the composition of claim 20.

30. The method of claim 29 wherein said administration is topical administration.

31. The method of claim 29 wherein said administration is parenteral administration.

32. The method of claim 29 wherein said administration is oral administration.

33. The method of claim 29 wherein said administration is rectal administration.

34. A method for the prevention and treatment of pruritus in a mammal in need of such prevention or treatment comprising administering to said mammal an effective anti-pruritic amount of the composition of claim 21.

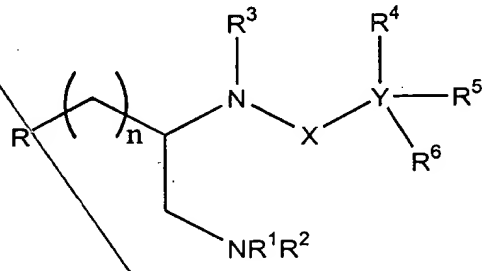
35. The method of claim 34 wherein said administration is topical administration.

36. The method of claim 34 wherein said administration is parenteral administration.

37. The method of claim 34 wherein said administration is oral administration.

38 The method of claim 34 wherein said administration is rectal administration.

39. An anti-pruritic pharmaceutical composition comprising a compound of formula III or a pharmaceutically acceptable salt thereof



III

wherein

n is 0-1;

R is unsubstituted phenyl or phenyl substituted with one to three substituents selected from the group consisting of halogen, C_{1-6} alkyl, hydroxy, -O-CO-NH_2, -O-CO-NHalkyl, -O-CO-N(alkyl)$_2$, C_{1-6} alkoxy, trifluoromethyl, C_{1-4}-alkoxy-C_{1-4} alkyloxy, carboxy-C_{1-4} alkyloxy, nitrile, nitro and amino; or mono or dialkyl amino, amide, sulfonamide, carboxamide; or mono or disubstituted carboxamide, ureido, or mono and di-alkylsubstituted ureido; or

R represents an alkyl or cycloalkyl group having up to 7 carbon atoms, wherein the cycloalkyl moiety, where present, can be optionally substituted by one or more substituents selected from the group consisting of from hydroxy, amino, amidino, guanidino, aminocarbonyl, carboxy, C_{1-6} alkoxy, (C_{1-6} alkoxy)carbonyl, (C_{3-6} alkenyloxy)carbonyl, (C_{3-6} alkynyloxy)carbonyl, C_{1-6} alkanoyloxy, C_{1-6} alkylsulfide, C_{1-6} alkylsulfoxide, C_{1-6} alkylsulfone, C_{1-6}(monoalkylamino)carbonyl, C_{1-6} acylamino, C_{1-6} acylmethylamino and C_{1-6} monoalkylamino; or

R represents the group -B-R^7 in which B represents -CH_2-, -$CH(CH_3)$- or a single bond and R^7 represents an optionally substituted C_{6-10} carbocyclic aryl group with one to three substituents selected from the group consisting of halogen, C_{1-6} alkyl, hydroxy, -O-CO-NH_2, -O-CO-NHalkyl, -O-CO-N(alkyl)$_2$, C_{1-6} alkoxy, trifluoromethyl, C_{1-4}-alkoxy-C_{1-4} alkyloxy, carboxy-C_{1-4} alkyloxy, nitrile, nitro and amino; or mono or dialkyl amino, amide, sulfonamide, carboxamide; mono or disubstituted carboxamide ureido; and mono or di-alkylsubstituted ureido; or

R represents the group -D-R^8 in which D represents a single bond, -CH_2-, -$CH(CH_3)$-, -CH_2O-, -$CH(CH_3)O$-, -CH_2S-, -$CH(CH_3)S$-, -CH_2NH- or -$CH(CH_3)NH$- and R^8 represents a 4-6 membered heterocyclic ring containing up to 4 heteroatoms selected from the group consisting of oxygen, sulfur and nitrogen, the heterocyclic ring optionally being substituted on nitrogen or sulfur by oxygen or on nitrogen by hydroxy or C_{1-3} alkyl and/or the ring optionally being substituted on carbon by one or more substituents selected from the group consisting of amino, hydroxy, thio (and their tautomers), cyano, halogen, C_{1-3} alkoxy, C_{1-3} monoalkylamino, C_{1-3} acylamino, C_{1-3} acylmethylamino, and C_{1-3} alkylthio;

R^1 and R^2 are independently selected from the group consisting of H, C_{1-6} alkyl, C_{3-5} alkenyl, C_{3-5} alkynyl, and C_{4-7} cycloalkylalkyl group; or R^2 can be taken together with R^1 and the nitrogen to which they are attached to form a heterocyclic ring which may optionally contain a further heteroatom selected from the group consisting of oxygen, nitrogen, and sulfur, said heterocyclic ring selected from the gorup consisting of 1-azetidinyl and 1-pyrrolidinyl said 1-pyrrolidinyl optionally substituted at the 3-position by OH, -CH_2OH, tri(C_1-C_6 alkyl)silyloxy, acyloxy, C_{1-6} alkyl, C_{1-6} alkoxy or C_{1-6} alkanoyloxy; 1-piperazinyl optionally substituted at the 4-position by alkyl of 1 to 3 carbon atoms; 1-morpholino; 2,5-dihydro-1H-pyrrol-1-yl; 3-azabicyclo[3.1.0]hexan-3-yl; or 3-azabicyclo[3.2.0]heptan-3-yl;

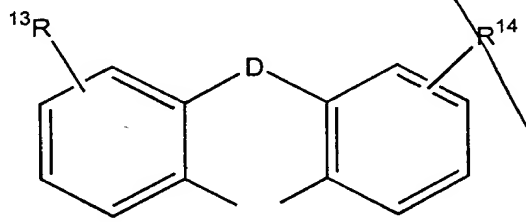
R^3 represents hydrogen, C_{1-7} alkyl, -CH_2-phenyl or heterocyclic wherein the phenyl or heterocyclic groups may be substituted with one to three substituents selected from the group consisting of halo, C_{1-4} alkyl, C_{1-4} alkoxy and methoxycarbonyl; mono-, di- or trihalomethyl; cyano; COR^9, $CH{=}NOR^{10}$, OR^{10}, SR^{10}, CH_2CN, CH_2OR^{10}, CH_2SR^{10}, $CH_2S(O)R^{10}$, $CH_2S(O)_2R^{10}$, $CH_2N(R^{10})R^{11}$, $CH_2(R^{10})R^{11}$, $CH_2NR^{10}OH$, $CH_2N(COR^{10})OH$,

$CH_2NR^{10}COR^{11}$, $CH_2NR^{10}S(O)_2R^{11}$, or CH_2OCOR^{10}, wherein R^9 is hydrogen, hydroxy, amino, NHOH, $NHOCH_3$, pyridylamino, $NHN(CH_3)_2$, C_{1-4} alkoxy, benzyloxy, C_{1-4} alkylamino, di-C_{1-4} alkylamino, C_{1-4} alkyl or C_{1-4} alkylthio; R^{10} and R^{11} are each hydrogen, C_{1-4} alkyl, C_{1-4} alkoxy or C_{7-11} phenylalkyl), or OR^{12}, wherein R^{12} is hydrogen, C_{1-4} alkyl or a hydroxy protecting group;

X represents -CO-, or $-SO_2-$;

Y represents a single bond wherein only one of R^4-R^6 is attached, a tetrahedral carbon, -OC-, -SC-, -S(O)C-, $-S(O)_2C-$, or $-CH_2C-$;

R^4, R^5, and R^6 are independently selected from the group consisting of hydrogen, hydroxy, alkoxy, C_{1-4} alkylenedioxy, C_{1-8} cyclic and acyclic alkyl; substituted or unsubstituted carbocyclic aromatic or heterocyclic aromatic group selected from the group consisting of phenyl, naphthyl, biphenyl, indanyl, 1-tetralone-6-yl, furyl, thienyl, pyridyl, thiazolyl, benzofuryl and benzothienyl, each of which may be substituted with one to three substituents selected from the group consisting of halo, cyano, $-OCONH_2$, -OCONHalkyl, $-OCON(alkyl)_2$, -OCOalkyl, -NHCHO, -NHCOalkyl, ureido, -NHCONHalkyl, -NalkylCONHalkyl, $-NHCON(alkyl)_2$, $-NalkylCON(alkyl)_2$, $-NHSO_2alkyl$, -COalkyl, $-CONH_2$, -CONHalkyl, $-CON(alkyl)_2$, $-CH_2CONH_2$, $-CH_2CONHalkyl$, $-CH_2CON(alkyl)_2$, $-OCH_2CONH_2$, -$OCH_2CONHalkyl$, $-OCH_2CON(alkyl)_2$, C_{1-4} alkyl, C_{1-4} alkoxy, amino, hydroxy, nitro, trifluoromethyl, $-SO_2alkyl$, -SOalkyl, and mesyl; or R^5 and R^6 can together form the following structure



wherein R^{13} and R^{14} are independently selected from the group consisting of hydrogen, halogen, hydroxy, alkoxy, mono-, di- or tri-halomethyl, amino, -NHalkyl, $-N(alkyl)_2$, -NHCOalkyl, ureido, nitro, and methylenedioxy; and

D represents $-CH_2-$, -O-, -S-, -NH, $-CH_2CH_2-$, -CH=CH-, $-CH_2NH-$, or $-CH_2$Nalkyl-; in a pharmaceutically carrier.

40. The anti-pruritic pharmaceutical composition of Claim 39 wherein said compound is selected form the group consisting of:

N-methyl-N-{[1S]-1-phenyl-2-[(3S)-(3-hydroxypyrrolidin-1-yl)]ethyl}-2,2-diphenylacetamide hydrochloride,

3,4-dichloro-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]benzeneacetamide hydrochloride,

N-methyl-N-{[1S]-1-phenyl-2-[(3S)-(3-hydroxypyrrolidin-1-yl)]ethyl}-2-aminophenylacetamide hydrochloride,

3,4-dichloro-N-methyl-N-[(1S)-1-isopropyl-2-(1-pyrrolidinyl)ethyl]benzeneacetamide hydrochloride,

3,4-dichloro-N-methyl-N-[(1S)-1-(O-acetic acid-3-hydroxyphenyl)-2-(1-pyrrolidinyl)ethyl]benzeneacetamide hydrochloride, and

N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]-2,2-diphenylacetamide hydrochloride.

41. A method for the prevention or treatment of pruritus in a mammal in need of such prevention or treatment comprising administering to said mammal an effective anti-pruritic amount of the composition of claim 39.

42. The method of claim 41 wherein said administration is topical administration.

43. The method of claim 41 wherein said administration is parenteral administration.

44. The method of claim 41 wherein said administration is oral administration.

45. The method of claim 41 wherein said administration is rectal administration.

46. A method for the prevention or treatment of pruritus in a mammal in need of such prevention or treatment comprising administering to said mammal an effective anti-pruritic amount of the composition of claim 40.

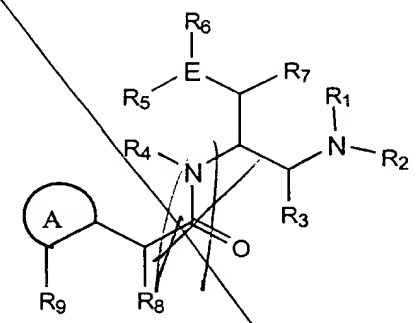
47. The method of claim 46 wherein said administration is topical administration.

48. The method of claim 46 wherein said administration is parenteral administration.

49. The method of claim 46 wherein said administration is oral administration.

50. The method of claim 46 wherein said administration is rectal administration.

51. An anti-pruritic pharmaceutical composition comprising a compound of formula IV or a pharmaceutically acceptable salt thereof



IV

wherein:

R_1 and R_2 are the same or different and are hydrogen, C_{1-6} alkyl, C_{3-6} alkenyl, C_{3-6} cycloalkyl or C_{4-12} cycloalkylalkyl groups, or R_1 and R_2 together form a C_{2-8} branched or linear polymethylene or C_{2-6} alkenylene group, each of which may be optionally substituted with a hetero-atom; or $-NR_1R_2$ forms a 5-membered (optionally containing an oxygen atom adjacent to the nitrogen) or 6-membered ring, which rings optionally contains one unit of unsaturation and which is unsubstituted or substitued with hydroxy, C_{1-6} acyloxy, oxo, methylene, $-COR_{10}$ where R_{10} represents C_{1-6} alkyl, $-OR_{11}$ or $-NHR_{11}$ and R_{11} represents hydrogen, C_{1-6} alkyl, aryl, $Ar(C_{1-6})$alkyl, or $N=NOR_{12}$ (where R_{12} represents C_{1-6} alkyl;

R_3 is hydrogen, C_{1-6} alkyl; or phenyl; or R_3 together with R_1 form a $-(CH_2)_3-$ or $-(CH_2)_4-$ group;

R_4 is C_{1-6} alkyl, or phenyl;

R_5 is hydrogen, or together with R_4 forms a C_{2-5} linear polymethylene group;

R_6 represents hydroxy, C_{1-6} alkyl, C_{1-6} hydroxyalkyl, C_{1-6} carboxyalkyl, phenyl, oxo,amino, carboxy, amido, $-COR_{13}$, $-CO_2R_{13}$ or $-COCO_2R_{13}$ where R_{13} represents a hydrogen atom or an unsubstituted or substituted C_{1-10} hydrocarbon moiety; -NRxCORx where Rx represents C_{1-6} alkyl, optionally substituted methylene or R_6 together with the E atom to which it is attached, forms a 5 or 6-membered ring containing one or more heteroatoms;

R_7 is hydrogen, or together with R_6 forms an optionally substituted or unsubstituted single or fused aryl or heterocyclic ring, containing from 5 to 12 ring atoms and comprising up to four heteroatoms in the ring selected from the group consisting of oxygen, nitrogen and sulphur, which may be substituted with hydrogen, C_{1-6} alkyl, $-CH_2OR_{14}$, halogen, hydroxy, C_{1-6} alkoxy, C_{1-6} alkoxycarbonyl, thiol, C_{1-6} alkylthio, $-OCOR_{15}$, $-NHCOR_{16}$, $-NHSO_2R_{17}$ or $-CH_2SO_2NR_{18}R_{19}$, in which each of R_{14} to R_{19} is independently hydrogen, C_{1-6} alkyl, aryl or aralkyl;

A is aryl or heteroaryl ring, optionally mono or disubstituted with C_{1-6} alkyl, C_{2-6} alkenyl, C_{1-6} haloalkyl , C_{2-6} haloalkenyl, C_{2-6} haloalkynyl, aryl, aralkyl, hydroxy, C_{1-6} alkoxy, C_{1-6} haloalkoxy, thiol, C_{1-6} alkylthio, C_{1-6} haloalkylthio, halogen, nitro, cyano, carboxy, aryloxy, aralkoxycarbonyl, carbamoyl, sulfonyl or sulfamoyl;

E represents methylene, sulphur, oxygen or an imino group;

R_8 is hydrogen or C_{1-6} alkyl; and

R_9 is hydrogen or together with R_8may form the group -(CRaRa)m-C(=Y)- wherein Ra is hydrogen or C_{1-6} alkyl having up to a maximum of 3 alkyl groups;

m is 1, 2, or 3; and

Y represents two hydrogens or oxygen,

in a pharmaceutically acceptable vehicle.

52. The anti-pruritic pharmaceutical composition of claim 51 wherein said compound is selected form the group consisting of:

1-(Pyrrolidin-1-yl)methyl-2-(3,4-dichlorophenyl)-acetyl-4,4-dimethyl-1,2,3,4-tetrahydroisoquinoline;

8-[(3,4-Dichlorophenyl)acetyl]-7-(1-pyrrolidinylmethyl)-1,4-dioxa-8-aza[4.5]spirodecane;

Methyl 4-[3,4-dichlorophenyl)acetyl]-3-(1-pyrrolidinylmethyl)-1-piperazinecarboxylate

1-[(3,4-Dichlorophenyl)acetyl]-2-[(3-oxo-1-pyrolidinyl)methyl]-piperidine.

[S-(RR)]-(-)5-[(3,4-Dichlorophenyl)acetyl]-4,5,6,7-tetrahydro-4[(3-hydroxy-1-pyrolidinyl)methyl]furo[3,2-c]pyridine;

[S-(RS)]-4-Acetyl-1-[(3,4-dichlorophenyl)acetyl]-2-[(3-hydroxy-1-pyrolidinyl)methyl]pyridine;

2-[(3,4-Dichlorophenyl)acetyl]-1,2,3,4-tetrahydro-1-(1-pyrolidinyl)methyl)-5-isoquinolinol;.

4-(Pyrolidin-1-yl)methyl-5-(3,4-dichlorophenyl)acetyl-4,5,6,7-tetrahydrothieno[3,2,-c]pyridine;

1-[(5,6-Dichloro-3-oxoindan-1-carbonyl)-2-pyrrolidin-1-ylmethyl)piperidine;

2-(3,4-Dichlorophenyl)acetyl-3-(pyridin-1-yl)methyl-decahydroisoquinoline;

1-(4-Trifluoromethylphenyl)acetyl-2-(3-hydroxypyrolidin-1-yl)methyl-4,4-dimethyl piperidine;

4-Acetyl-1-[(3,4-dichlorophenyl)acetyl]-2-[(S)-3-hydroxy-1-pyrrolidinyl)methyl]piperazine;

4-Acetyl-1-[(4-methylsulphonylphenyl)acetyl]-2-[(S)-3-hydroxy-1-pyrrolidinyl)methyl]piperazine;

4-(2-Ethanol)-1-[(3,4-dichlorophenyl)acetyl]-2-[(S)-3-hydroxy-1-pyrrolidinyl)methyl]piperazine;

4-Spirohydantoin-1-[(3,4-dichlorophenyl)acetyl]-2-[(pyrrolidinyl)methyl]piperazine; and

4-[(S)-3-hydroxy-1-pyrrolidinyl)methyl]-5-[3,4-dichlorophenyl)acetyl]-4,5,6,7-tetrahydroimidazo [4,5-c]pyridine.

53. A method for the prevention or treatment of pruritus in a mammal in need of such prevention or treatment comprising administering to said mammal an effective anti-pruritic amount of the composition of claim 51.

54. The method of claim 53 wherein said administration is topical administration.

55. The method of claim 53 wherein said administration is parenteral administration.

56. The method of claim 53 wherein said administration is oral administration.

57. The method of claim 53 wherein said administration is rectal administration.

58. A method for the prevention or treatment of pruritus in a mammal in need of such prevention or treatment comprising administering to said mammal an effective anti-pruritic amount of the composition of claim 52.

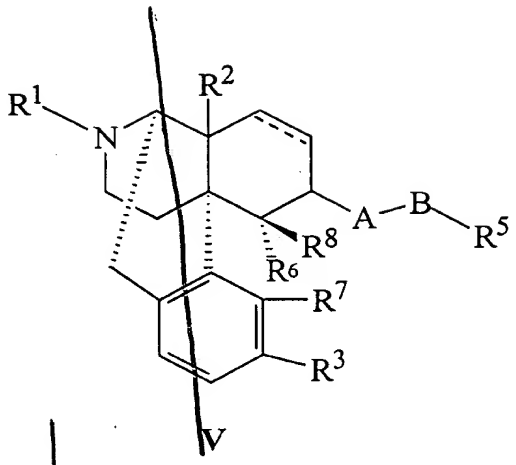
59. The method of claim 58 wherein said administration is topical administration.

60. The method of claim 58 wherein said administration is parenteral administration.

61. The method of claim 58 wherein said administration is oral administration.

62. The method of claim 58 wherein said administration is rectal administration.

63. An anti-pruritic pharmaceutical composition comprising a compound of formula V or a pharmaceutically acceptable salt thereof



wherein

----- represents a single or double bond;

R^1 represents an alkyl group having 1-5 carbon atoms, a cycloalkylalkyl group having 4-7 carbon atoms, a cycloalkenylalkyl group having 5-7 carbon atoms, an aryl group having 6-12 carbon atoms, an aralkyl group having 7-13 carbon atoms, an alkenyl group having 4-7 carbon atoms, an allyl group, a furan-2-ylalkyl group having 1-5 carbon atoms, or a thiophen-2-ylalkyl group having 1-5 carbon atoms;

R^2 represents a hydrogen atom, a hydroxy group, a nitro group, an alkanoyloxy group having 1-5 carbon atoms, an alkoxy group having 1-5 carbon atoms, an alkyl group having 1-5 carbon atoms, or $-NR^9R^{10}$ wherein R^9 represents a hydrogen atom or an alkyl group having 1-5 carbon atoms, and R^{10} represents a hydrogen atom; an alkyl group having 1-5 carbon atoms, or $-C(=O)R^{11}$ wherein R^{11} represents a hydrogen atom, a phenyl group or an alkyl group having 1-5 carbon atoms;

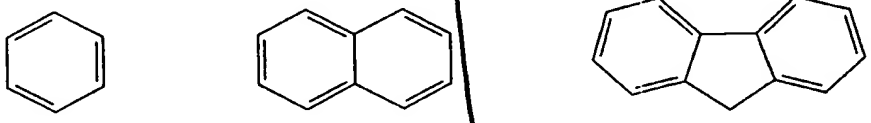
R^3 represents a hydrogen atom, a hydroxy group, an alkanoyloxy group having 1-5 carbon atoms, or an alkoxy group having 1-5 carbon atoms;

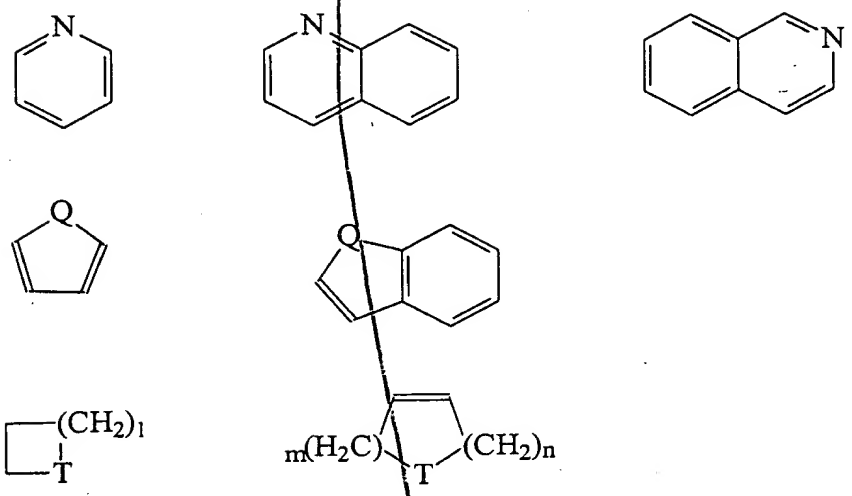
A represents $-XC(=Y)-$, $-XC(=Y)Z-$, $-X-$, $-XSO_2-$, or $-OC(OR^4)R^4-$ where, X, Y and Z each independently represent NR^4, S or O wherein R^4 represents a hydrogen atom, a straight-chain or branched chain alkyl group having 1-5 carbon atoms or an aryl group having 6-12 carbon atoms, and wherein R^4 may be identical or different;

B represents a valence bond, a straight-chain or branched chain alkylene group having 1-14 carbon atoms which may be substituted with at least one substituent selected from the group consisting of an alkoxy group having 1-5 carbon atoms, an alkanoyloxy group having 1-5 carbon atoms, a hydroxy group, fluorine, chlorine, bromine, iodine, an amino group, a nitro group, a cyano group, a trifluoromethyl group and a phenoxy group, and wherein 1 to 3 methylene groups may be replaced with carbonyl groups, an acyclic unsaturated hydrocarbon containing from 1 to 3 double bonds and/or triple bonds and having 2-14 carbon atoms which may be substituted with at least one substituent group selected from the group consisting of an alkoxy group having 1-5 carbon atoms, an alkanoyloxy group having 1-5 carbon atoms, a hydroxy group, fluorine, chlorine, bromine, iodine, an amino group, a nitro group, a cyano group, a trifluoromethyl group and a phenoxy group, and wherein from 1 to 3 methylene groups may be replaced with carbonyl groups, or a straight-chain or branched chain saturated or unsaturated hydrocarbon group containing from 1 to 5 thioether, ether and/or amino bonds and having 1-14 carbon atoms wherein hetero atoms are not bonded directly to A, and 1 to 3 methylene groups may be replaced with carbonyl groups;

R^5 represents a hydrogen atom or an organic group (which may be substituted with at least one or more substituent groups selected from the group consisting of an alkyl group having 1-5 carbon atoms, an alkoxy group having 1-5 carbon atoms, an alkanoyloxy group having 1-5 carbon atoms, a hydroxy group, fluorine, chlorine, bromine, iodine, an amino group, a nitro group, a cyano group, an isothiocyanate group, a trifluoromethyl group and a methylenedioxy group); or

R_5 is





wherein
Q is N, O or S;

T is CH, N, S or O;

l is 0-5;

m and n are ≥ 0

$m + n \leq 5$;

R^6 represents a hydrogen atom;

R^7 represents a hydrogen atom, a hydroxy group, an alkoxy group having 1-5 carbon atoms, an alkanoyloxy group having 1-5 carbon atoms, or R^6 and R^7 together represent -O-, $-CH_2-$ or -S-;

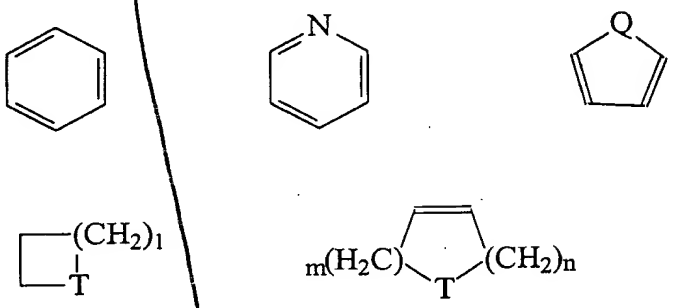
R^8 represents a hydrogen atom, an alkyl group having 1-5 carbon atoms, or an alkanoyl group having 1-5 carbon atoms in a pharmaceutically acceptable carrier.

64. The anti-pruritic pharmaceutical composition of claim 63 wherein

R^1 is an alkyl group having 1-5 carbon atoms, a cycloalkylmethyl group having 4-7 carbon atoms, a cycloalkenylmethyl group having 5-7 carbon atoms, a phenylalkyl group having 7-13 carbon atoms, an alkenyl group having 4-7 carbon atoms, an allyl group, a furan-2-yl-alkyl group having 1-5 carbon atoms and a thiophen-2-yi-alkyl group having 1-5 carbon atoms;

R^2 is hydrogen, hydroxy, nitro, acetoxy, methoxy, methyl, ethyl, propyl, amino, dimethylamino, acetylamino or benzoylamino groups; or

R^4 is



Formula V-1

wherein

Q is N, O or S;

T is CH, N, S or O;

m and n are ≥ 0 and

$m + n \leq 5$;

B is $-(CH_2)_n-$ wherein n = 0-6, $-(CH_2)_n-C(=O)-$ wherein n = 1-4, $-CH=CH-(CH_2)_n-$ wherein n = 0-4, $-C\equiv C-(CH_2)_n-$ wherein n=0-4, $-CH_2-O-$, $-CH_2-S-$, $-CH_2-O-(CH_2)_2-O-(CH_2)_2-$, $-CH_2-O-CH_2-NH-CH_2-O-CH_2-$ and $-CH_2-O-CH_2-S-CH_2-O-CH_2-$;

R^5 is hydrogen or an organic group of Formula V-1 said organic group may be substituted with at least one substituent group selected from the group consisting of an alkyl group having 1-5 carbon atoms, an alkoxy group having 1-5 carbon atoms, an alkanoyloxy group having 1-5 carbon atoms, a hydroxy group, fluorine, chlorine, bromine, an amino group, a nitro group, a cyano group, an isothiocyanate group and a trifluoromethyl group, in a pharmaceutically acceptable carrier.

65. The anti-pruritic pharmaceutical composition of claim 64 wherein

R^1 is methyl, ethyl, cyclopropylmethyl, cyclobutylmethyl, cyclopentylmethyl, cyclopentenylmethyl, cyclohexenylmethyl, benzyl, phenethyl, trans-2-butenyl, 2-methyl-2-butenyl, allyl, furan-2-yl-methyl or thiophen-2-yl-methyl;

R^2 is hydrogen, hydroxy, nitro, acetoxy, methyl or dimethylamino;

R^3 is $-NR^4C(=O)-$, $-NR^4C(=S)-$, $-NR^4C(=O)O-$, $-NR^4C(=O)NR^4-$, $-NR^4C(=S)NR^4-$ or $-NR^4SO_2-$;

R^4 is a straight-chain or branched alkyl group having 1-5 carbon atoms;

B is $-(CH_2)_n-$ wherein n=0-6, $-CH=CH(CH_2)_n-$ wherein n=0-4, $-C\equiv C-(CH_2)_n-$ wherein n=0-4, $-CH_2-O-$ or $-CH_2-S-$; and

R^5 is hydrogen, phenyl, 3,4-dichlorophenyl, 4-chlorophenyl, 3-chlorophenyl, 3,4-difluorophenyl, 4-fluorophenyl, 3-fluorophenyl, 2-fluorophenyl, 4bromophonyl, 3-bromophenyl, 2-bromophenyl, 4-nitrophenyl, 3-nitrophenyl, 2-nitrophenyl, 4-trifluoromethylphenyl, 3-trifluoromethylphenyl, 2-trifluoromethylphenyl, 4-methylphenyl, 3-methylphenyl, 2-methylphenyl, 4-methoxyphenyl, 3-methoxyphenyl, 2-mothoxy, 3-furanyl, 2-furanyl, 3-thienyl, 2-thienyl, cyclopentyl or cyclohexyl, in a pharmaceutically acceptable carrier.

66. The anti-pruritic pharmaceutical composition of claim 65 wherein said compound is selected from the group consisting of:

17-cyclopropylmethyl-4,5α-epoxy-3,14β-dihydroxy-6β-(N-methyl-3-phenylpropionamido)morphinan;

17-cyclopropylmethyl-4,5α-epoxy-3,14β-dihydroxy-6β-(N-methyl-trans-3-(3-furyl)acrylamido)morphinan;

17-cyclopropylmethyl-4,5α-epoxy-3,14β-dihydroxy-6β-(N-methyl-trans-3-cyclohexylacrylamido)morphinan;

17-cyclopropylmethyl-4,5α-epoxy-3,14β-dihydroxy-6β-(N-methyl-trans-3-(4-trifluoromethylphenyl)acrylamido)morphinan;

17-cyclopropylmethyl-4,5α-epoxy-3,14β-dihydroxy-6α-(N-methyl-trans-3-(3-thiophenyl)acrylamido)morphinan;

17-cyclopropylmethyl-4,5α-epoxy-3,14β-dihydroxy-6β-(N-methyl-trans-3-phenylacrylamido)morphinan;

17-cyclopropylmethyl-4,5α-epoxy-3,14β-dihydroxy-6β-(N-methyl-trans-2-hexenamido)morphinan; and

17-cyclopropylmethyl-4,5α-epoxy-3,14β-dihydroxy-6β-(N-methyl-phenylpropiolamido)morphinan

67. A method for the prevention or treatment of pruritus in a mammal in need of such prevention or treatment comprising administering to said mammal an effective anti-pruritic amount of the composition of claim 63.

68. The method of claim 67 wherein said administration is topical administration.

69. The method of claim 67 wherein said administration is parenteral administration.

70. The method of claim 67 wherein said administration is oral administration.

71. The method of claim 67 wherein said administration is rectal administration.

72. A method for the prevention or treatment of pruritus in a mammal in need of such prevention or treatment comprising administering to said mammal an effective anti-pruritic amount of the composition of claim 64.

73. The method of claim 72 wherein said administration is topical administration.

74. The method of claim 72 wherein said administration is parenteral administration.

75. The method of claim 72 wherein said administration is oral administration.

76. The method of claim 72 wherein said administration is rectal administration.

77. A method for the prevention or treatment of pruritus in a mammal in need of such prevention or treatment comprising administering to said mammal an effective anti-pruritic amount of the composition of claim 65.

78. The method of claim 77 wherein said administration is topical administration.

79. The method of claim 77 wherein said administration is parenteral administration.

80. The method of claim 77 wherein said administration is oral administration.

81. The method of claim 77 wherein said administration is rectal administration.

82. A method for the prevention or treatment of pruritus in a mammal in need of such prevention or treatment comprising administering to said mammal an effective anti-pruritic amount of the composition of claim 66.

83. The method of 82 wherein said administration is topical administration.

84. The method of claim 82 wherein said administration is parenteral administration.

85. The method of claim 82 wherein said administration is oral administration.

86. The method of claim 82 wherein said administration is rectal administration.

53